FILE 'EMBASE, BIOSIS, SCISEARCH, MEDLINE, CAPLUS' ENTERED AT 13:53:21 ON 10 MAY 2005

L2	5365	S	APTAMER
L3	22	S	FIRST (W) BINDING (W) DOMAIN
L4	39	S	SECOND (W) BINDING (W) DOMAIN
L5	0	S	L2 AND L3 AND L4
L6	0	S	L2 AND L3
L7	2	S	L2 AND BIVALENT (W) BINDING (W) MOLECULE
L8	1261398	S	L2 AND AGONIST OR ANTAGONIST
L9	39	S	L2 AND AGONIST
L10	304	S	L2 AND ANTAGONIST
L11	17	S	L2 AND BIVALENT
L12	2	DUP REM	L7 (0 DUPLICATES REMOVED)
L13	29	DUP REM	L9 (10 DUPLICATES REMOVED)
L14	9	DUP REM	L11 (8 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 13:58:16 ON 10 MAY 2005

FILE 'CAPLUS' ENTERED AT 13:59:47 ON 10 MAY 2005

FILE 'STNGUIDE' ENTERED AT 13:59:47 ON 10 MAY 2005

FILE 'EMBASE, BIOSIS, SCISEARCH, MEDLINE, CAPLUS' ENTERED AT 14:01:18 ON 10 MAY 2005

FILE 'STNGUIDE' ENTERED AT 14:01:23 ON 10 MAY 2005

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FILE 'MEDLINE' ENTERED AT 13:53:21 ON 10 MAY 2005

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=> s aptamer
L2        5365 APTAMER

=> s first (w) binding (w) domain
L3          22 FIRST (W) BINDING (W) DOMAIN

=> s second (w) binding (w) domain
L4          39 SECOND (W) BINDING (W) DOMAIN

=> s l2 and l3 and l4
L5           0 L2 AND L3 AND L4

=> s l2 and l3
L6           0 L2 AND L3

=> s l2 and bivalent (w) binding (w) molecule
L7           2 L2 AND BIVALENT (W) BINDING (W) MOLECULE

=> s l2 and agonist or antagonist
L8     1261398 L2 AND AGONIST OR ANTAGONIST

=> s l2 and agonist
L9          39 L2 AND AGONIST

=> s l2 and antagonist
L10        304 L2 AND ANTAGONIST

=> s l2 and bivalent
L11         17 L2 AND BIVALENT

=> dup rem l7
PROCESSING COMPLETED FOR L7
L12           2 DUP REM L7 (0 DUPLICATES REMOVED)

=> dup rem l9
PROCESSING COMPLETED FOR L9
L13          29 DUP REM L9 (10 DUPLICATES REMOVED)

=> dup rem l11
PROCESSING COMPLETED FOR L11
L14           9 DUP REM L11 (8 DUPLICATES REMOVED)

=> d l2 iall

L2   ANSWER 1 OF 5365  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS
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RESERVED. on STN

ACCESSION NUMBER: 2005170456 EMBASE

TITLE: Allosteric **aptamers** and aptazymes as probes for screening approaches.

AUTHOR: Famulok M.

CORPORATE SOURCE: M. Famulok, Rheinische Friedrich-Wilhelms-Univ., Kekule Inst. Organ. Chem./Biochemie, Gerhard-Domagk-Strasse 1, Bonn 53121, Germany. m.famulok@uni-bonn.de

SOURCE: Current Opinion in Molecular Therapeutics, (2005) Vol. 7, No. 2, pp. 137-143.
Refs: 58
ISSN: 1464-8431 CODEN: CUOTFO

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20050428
Last Updated on STN: 20050428

ABSTRACT: Substantial effort is currently being devoted to engineering allosteric nucleic acids, **aptamers** and ribozymes for various applications in cellular and molecular biology, biotechnology and diagnostics. These molecular switches alter their different functional activities in response to specific binding molecules, including proteins, nucleic acids and small organic compounds. The interacting molecules trigger a response in the allosteric nucleic acid, which can be used for purposes such as real-time monitoring, high-throughput screening orgene expression control. .COPYRGT. The Thomson Corporation.

CONTROLLED TERM: Medical Descriptors:
allosterism
cytology
molecular biology
biotechnological procedures
diagnostic procedure
protein binding
high throughput screening
gene expression
reverse transcription polymerase chain reaction
ligand binding
in vitro study
in vivo study
Human immunodeficiency virus 1
enzyme activity
protein phosphorylation
mammal cell
transcription regulation
Neurospora crassa
Saccharomyces cerevisiae
Schistosoma mansoni
Escherichia coli
molecular probe
nonhuman
review
Drug Descriptors:
***aptamer**
nucleic acid
ribozyme
organic compound
adenosine triphosphate
flavine mononucleotide
green fluorescent protein

luciferase
Rev protein: EC, endogenous compound
self splicing ribosomal RNA
beta galactosidase: EC, endogenous compound

CAS REGISTRY NO.: (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5; (flavine mononucleotide) 130-40-5, 146-17-8; (luciferase) 61970-00-1, 9014-00-0; (Rev protein) 111804-97-8, 127004-89-1

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	41.64	43.03

FILE 'STNGUIDE' ENTERED AT 13:58:16 ON 10 MAY 2005

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 6, 2005 (20050506/UP).

=> d 1-2 l12 iall
YOU HAVE REQUESTED DATA FROM FILE 'CAPLUS' - CONTINUE? (Y)/N:y

L12 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:70006 CAPLUS
DOCUMENT NUMBER: 140:123646
ENTRY DATE: Entered STN: 28 Jan 2004
TITLE: Method of screening for bivalent binding nucleic acid ligands (**aptamers**) of 7 transmembrane G protein-coupled receptors for therapeutic and diagnostic use
INVENTOR(S): Gold, Larry
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: U.S., 17 pp., Cont.-in-part of U.S. Ser. No. 956,699.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C12Q001-68
SECONDARY: C12P019-34
US PATENT CLASSIF.: 435006000; 435091200; 935077000; 935078000; 536023100; 536025400
CLASSIFICATION: 3-1 (Biochemical Genetics)
Section cross-reference(s): 2, 9, 63
FAMILY ACC. NUM. COUNT: 127
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6682886	B1	20040127	US 1998-118525	19980717
US 5683867	A	19971104	US 1994-234997	19940428
US 6083696	A	20000704	US 1997-956699	19971023
WO 2000004184	A1	20000127	WO 1999-US14853	19990630

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,

TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9947287	A1	20000207	AU 1999-47287		19990630
EP 1100960	A1	20010523	EP 1999-930840		19990630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AU 773741	B2	20040603	AU 2001-18257		20010202
AU 773815	B2	20040610	AU 2001-29834		20010323
US 2004091931	A1	20040513	US 2003-729667		20031205
PRIORITY APPLN. INFO.:			US 1994-234997	A1	19940428
			US 1997-956699	A2	19971023
			US 1990-536428	B2	19900611
			AU 1991-82061	A0	19910610
			US 1991-714131	A2	19910610
			US 1993-117991	B2	19930908
			US 1993-123935	B2	19930917
			US 1994-199507	A2	19940222
			US 1994-234797	A2	19940428
			AU 1996-58839	A3	19960530
			AU 1996-61611	A3	19960604
			US 1998-118525	A	19980717
			WO 1999-US14853	W	19990630

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6682886	ICM	C12Q001-68
	ICS	C12P019-34
	INCL	435006000; 435091200; 935077000; 935078000; 536023100; 536025400
US 6682886	NCL	435/006.000; 435/091.200; 536/023.100; 536/025.400
US 5683867	NCL	435/006.000; 435/091.200; 536/023.100; 536/025.400
	ECLA	C07H019/06E; C07H019/10E; C07H021/00C2; C07H021/00C4; C12N015/10C4; C12N015/11D; C12Q001/68A8+525/101; C12Q001/68A8; G01N033/532; G01N033/535; G01N033/68; G01N033/76
US 6083696	NCL	435/006.000; 435/091.200; 536/023.100; 536/024.300; 536/025.400
WO 2000004184	ECLA	C12Q001/68A8
US 2004091931	NCL	435/006.000; 435/007.100; 435/069.100; 435/320.100; 435/325.000; 530/350.000; 525/054.100; 530/395.000

ABSTRACT:
Methods for identifying and preparing **bivalent binding** ***mols.*** to 7 transmembrane domain containing G protein-coupled receptors, that can activate or inhibit 7 transmembrane G protein-coupled receptors, are described. SELEX (Systematic Evolution of Ligands by EXponential enrichment) method is used to screening high affinity nucleic acid ligands, also termed ***aptamers.*** It combines two or more binding domains to two or more different epitopes of the same 7 transmembrane G protein-coupled receptor. These SELEX-derived **bivalent binding mols.** comprise two or more binding domains which bind simultaneously to two or more epitopes of the same 7TM G protein-coupled receptor, thus has increased binding affinity to 7TM G protein-coupled receptor for their activation or inhibition. The method was exemplified by screening random RNA libraries for binding mols. to both ECL1 (extracellular loop 1) or ECL2 of neurokinin receptor NK1R using peptide affinity columns. The bivalent ligands, derived from two ECL1- and ECL1-binding RNA libraries by linking them through overlap-extension PCR reaction, can be enriched after cycles of SELEX process to generate double-stranded DNA templates for their future synthesis. These ***bivalent*** **binding mols.** may be useful as therapeutic and diagnostic agents.

SUPPL. TERM: drug screening bivalent **aptamer** 7TM G protein coupled receptor

INDEX TERM: Neurotensin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A, of human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Parathyroid hormone receptors
Secretin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A, of rat/opossum, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adenosine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A1, of rat or human or canine, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adenosine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A2B, of rat or human or sheep, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adenosine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A3, of human or sheep, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Bradykinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(B2, of human/rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Cholecystokinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(CCKA, of human/rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Cholecystokinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(CCKB, of canine or human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological

study); USES (Uses)
(D1, of rat or human or rhesus, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D1A, of rat or human or rhesus, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D2, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D3, of rat or human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D4, of human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D5, of rat or human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(GP2-7 or 5A or 5A(S12) or 5B, of mouse/human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Histamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(H1, of bovine, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Histamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(H2, of rat or canine or human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M1, of mouse or human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M2, of human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M3, of human, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M4, of human or chicken, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M5, of human/rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Oligonucleotides
ROLE: BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(RNA **aptamers**, binding to G protein coupled-receptor epitopes; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Genetic methods
(SELEX; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR1, of rat/human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR2, of mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR3, of rat/human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR4, of human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR5, of human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Polysiloxanes, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(amino, **aptamers** linked by; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Angiotensin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(angiotensin II, of human/rat/mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Liposomes
(**aptamers** linked by; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Hydrocarbons, biological studies
Monosaccharides
Oligosaccharides, biological studies
Peptides, biological studies
Polynucleotides
Polyoxyalkylenes, biological studies
Proteins
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**aptamers** linked by; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Polysiloxanes, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hydroxy, **aptamers** linked by; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: DNA
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(linker, for generation of bivalent RNA ligands to G protein-coupled receptors epitopes; method of screening for bivalent binding **aptamers** of 7

transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Canis familiaris
Human
Mus
Rattus
(method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: G protein-coupled receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Epitopes
(of G protein-coupled receptors; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Thyrotropin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of canine/rat or human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Gonadotropin-releasing hormone receptor
VIP receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Gonadotropin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of human/rat/mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Calcitonin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of human/rat/pig, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Corticotropin releasing factor receptors
Glucagon receptors
Growth hormone-releasing hormone receptors
Neuropeptide Y receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of swine or Drosophila, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent

binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Affinity chromatography
(screening for bivalent ligand to G protein-coupled receptors epitopes; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Polysiloxanes, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(thio or carboxy-functionalized, **aptamers** linked by; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: PCR (polymerase chain reaction)
(to link G protein coupled receptor epitope ECL1- or ECL2-binding RNA mols.; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT1, 1C, of mouse/human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT1, of rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT1A, of rat/human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT1B, of rat/human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT1D, of canine/human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT1E, of rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT2, of rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT2B, of human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT3, of mouse, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT7, of rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Endothelin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type ETB, of human, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Tachykinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type NK1, of human/mouse/rat, screening for bivalent nuclear acid ligands binding to peptides of; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Opioid receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(κ-opioid, of human/rat/mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α1, of hamster or bovine, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α1D, of rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2, of human or mouse or fish, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2, of human or rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2A, of human or porcine or rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2B, of human or rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2C, of mouse or rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(β1, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(β2, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(β3, of rat or human or bovine, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Opioid receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(δ-opioid, of human/mouse, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane

GPCRs for therapeutic and diagnostic use)

INDEX TERM: Opioid receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(μ-opioid, of human/rat, screening for bivalent nuclear acid ligands binding to; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 9002-89-5, Ethenol, homopolymer 9003-01-4, 2-Propenoic acid homopolymer 9004-53-9, Dextrin 12619-70-4, Cyclodextrin 25322-68-3, Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy- 25322-69-4, Poly[oxy(methyl-1,2-ethanediyl)], α-hydro-ω-hydroxy-
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**aptamers** linked by; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 268720-50-9P, RNA (synthetic)
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(as ligands to G protein coupled-receptor; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 255916-21-3, L-Phenylalanine, L-histidyl-L-asparaginyl-L-α-glutamyl-L-tryptophyl-L-tyrosyl-L-tyrosylglycyl-L-leucyl-L-phenylalanyl-L-tyrosyl-L-cysteinyl-L-lysyl-
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(neurokinin receptor 1 extracellular loop 1; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 255916-22-4, L-Valine, L-threonyl-L-threonyl-L-α-glutamyl-L-threonyl-L-methionyl-L-prolyl-L-seryl-L-arginyl-L-valyl-L-valyl-L-cysteinyl-L-methionyl-L-isoleucyl-L-α-glutamyl-L-tryptophyl-L-prolyl-L-α-glutamyl-L-histidyl-L-prolyl-L-asparaginyl-L-lysyl-L-isoleucyl-L-tyrosyl-L-α-glutamyl-L-lysyl-
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(neurokinin receptor 1 extracellular loop 2; method of screening for bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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L12 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6682886	B1	20040127	US 1998-118525	19980717
AU 9947287	A1	20000207	AU 1999-47287	19990630
EP 1100960	A1	20010523	EP 1999-930840	19990630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AU 773741	B2	20040603	AU 2001-18257	20010202
AU 773815	B2	20040610	AU 2001-29834	20010323

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US 1998-118525	A	19980717
AU 1991-82061	A0	19910610
US 1994-234997	A1	19940428
AU 1996-58839	A3	19960530
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WO 2000004184	ECLA	C12Q001/68A8
US 6682886	NCL	435/006.000; 435/091.200; 536/023.100; 536/025.400

ABSTRACT:
Methods for identifying and preparing **bivalent binding** ***mols.*** to 7 transmembrane domain containing G protein-coupled receptors are described. The methods are based on the SELEX method (Systematic Evolution of Ligands by EXponential enrichment) for generating high affinity nucleic acid ligands, termed **aptamers**. It combines two or more binding domains to two or more different epitopes of the same 7 transmembrane G protein-coupled receptor. The method was exemplified by screening in the random RNA library for binding mols. to either ECL1 (extracellular loop 1) or ECL2 of neurokinin receptor NK1R using peptide affinity columns. The bivalent ligands, derived from two ECL1- and ECL1-binding RNA libraries by linking them through overlap-extension PCR reaction, can be enriched after cycles of SELEX process to generate double-stranded DNA templates for their future synthesis . These ***bivalent*** **binding mols.** may be useful as therapeutic and diagnostic agents.

SUPPL. TERM: biosynthesis screening **bivalent binding mol** G protein coupled receptor; **aptamers** bivalent substance P receptor NK1R SELEX

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1, 1C, of mouse/human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1, of rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1A, of rat/human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1B, of rat/human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1D, of canine/human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1E, of rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT2, of rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT2B, of human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT3, of mouse, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT7, of rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Neurotensin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A, of human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Parathyroid hormone receptors
Secretin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A, of rat/opossum, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adenosine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A1, of rat or human or canine, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adenosine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A2B, of rat or human or sheep, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G

protein-coupled receptors)

INDEX TERM: Adenosine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A3, of human or sheep, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Bradykinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(B2, of human/rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D1, of rat or human or rhesus, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D2, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D3, of rat or human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D4, of human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D5, of rat or human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Endothelin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(ETB, of human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(GP2-7 or 5A or 5A(S12) or 5B, of mouse/human, screening for bivalent nuclear acid ligands binding to peptides of;

synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Histamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(H1, of bovine, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Histamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(H2, of rat or canine or human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M1, of mouse or human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M2, of human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M3, of human, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M4, of human or chicken, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M5, of human/rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Tachykinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(NK1, of human/mouse/rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Oligonucleotides
ROLE: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL

(Biological study); PREP (Preparation)
(RNA **aptamers**, binding to G protein coupled-receptor epitopes; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Genetic methods
(SELEX; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR1, of rat/human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR2, of mouse, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR3, of rat/human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR4, of human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR5, of human/mouse, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Polysiloxanes, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(amino, **aptamers** linked by; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Angiotensin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(angiotensin II, of human/rat/mouse, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Liposomes
(**aptamers** linked by; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Hydrocarbons, biological studies
Monosaccharides

Oligosaccharides, biological studies
Peptides, biological studies
Polynucleotides
Polyoxyalkylenes, biological studies
Proteins, general, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**aptamers** linked by; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Cholecystokinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cholecystokinin A, of human/rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Cholecystokinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cholecystokinin B, of canine or human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Polysiloxanes, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hydroxy, **aptamers** linked by; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: DNA
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(linker, for generation of bivalent RNA ligands to G protein-coupled receptors epitopes; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Epitopes
(of G protein-coupled receptors; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Thyrotropin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of canine/rat or human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Gonadotropin-releasing hormone receptor
VIP receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of human, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Gonadotropin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of human/rat/mouse, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G

protein-coupled receptors)

INDEX TERM: Calcitonin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of human/rat/pig, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Corticotropin releasing factor receptors
Glucagon receptors
Growth hormone-releasing hormone receptors
Neuropeptide Y receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of rat, screening for bivalent nuclear acid ligands binding to peptides of; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of swine or Drosophila, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Affinity chromatography
(screening for bivalent ligand to G protein-coupled receptors epitopes; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: G protein-coupled receptors
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Polysiloxanes, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(thio or carboxy-functionalized, **aptamers** linked by; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: PCR (polymerase chain reaction)
(to link G protein coupled receptor epitope ECL1- or ECL2-binding RNA mols.; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Opioid receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(κ-opioid, of human/rat/mouse, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α1, of hamster or bovine, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological

study); USES (Uses)
(α1D, of rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2, D, of human or rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2, of human or mouse or fish, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2A, of human or porcine or rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2B, of human or rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2C, of mouse or rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(β1, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(β2, of rat or human or mouse, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(β3, of rat or human or bovine, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Opioid receptors

ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(δ-opioid, of human/mouse, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Opioid receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(μ-opioid, of human/rat, screening for bivalent nuclear acid ligands binding to; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 79-10-7D, 2-Propenoic acid, polymers 9002-89-5 9004-53-9, Dextrin 12619-70-4, Cyclodextrin 25322-68-3 25322-69-4
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**aptamers** linked by; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 268720-50-9P, RNA (synthetic)
ROLE: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(as ligands to G protein coupled-receptor; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 255916-21-3 255916-22-4
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(neurokinin receptor 1 NK1R epitope; synthesis and identification of bivalent binding RNA mols. to G protein-coupled receptors)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Bracht; US 5780449 A 1998 CAPLUS
(2) Gold; US 5270163 A 1993 CAPLUS
(3) Nieuwlandt; US 5648214 A 1997 CAPLUS
(4) Xu, W; Proc Natl Acad Sci USA 1996, V93, P7475 CAPLUS

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=> d 1-17 l11 iall
YOU HAVE REQUESTED DATA FROM FILE 'EMBASE, BIOSIS, SCISEARCH, MEDLINE, CAPLUS' -
CONTINUE? (Y)/N:
YOU HAVE REQUESTED DATA FROM FILE 'EMBASE, BIOSIS, SCISEARCH, MEDLINE, CAPLUS' -
CONTINUE? (Y)/N:y

L11 ANSWER 1 OF 17 EMBASE
on STN
ACCESSION NUMBER: 2003152968 EMBASE
TITLE: Yeast genetic selections to optimize RNA decoys for transcription factor NF-κB.
AUTHOR: Cassiday L.A.; Maher III L.J.
CORPORATE SOURCE: L.J. Maher III, Department of Biochemistry, Mayo Foundation, 200 First Street SW, Rochester, MN 55905, United States. maher@mayo.edu
SOURCE: Proceedings of the National Academy of Sciences of the

United States of America, (1 Apr 2003) Vol. 100, No. 7, pp. 3930-3935.
Refs: 25
ISSN: 0027-8424 CODEN: PNASA6

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030501
Last Updated on STN: 20030501

ABSTRACT: In vitro-selected RNA **aptamers** are potential inhibitors of disease-related proteins. Our laboratory previously isolated an RNA ***aptamer*** that binds with high affinity to human transcription factor NF-κB. This RNA **aptamer** competitively inhibits DNA binding by NF-κB in vitro and is recognized by its target protein in vivo in a yeast three-hybrid system. In the present study, yeast genetic selections were used to optimize the RNA **aptamer** for binding to NF-κB in the eukaryotic nucleus. Selection for improved binding to NF-κB from RNA libraries encoding (i) degenerate **aptamer** variants and (ii) sequences present at round 8 of 14 total rounds of in vitro selection yielded RNA ***aptamers*** with dramatically improved in vivo activity. Furthermore, we show that an in vivo-optimized RNA **aptamer** exhibits specific "decoy" activity, inhibiting transcriptional activation by its NF-κB target protein in a yeast one-hybrid assay. This decoy activity is enhanced by the expression of a **bivalent aptamer**. The combination of in vitro and in vivo genetic selections was crucial for obtaining RNA ***aptamers*** with in vivo decoy activity.

CONTROLLED TERM: Medical Descriptors:
*genetic selection
yeast
protein isolation
DNA binding
competitive inhibition
eukaryotic cell
cell nucleus
RNA sequence
protein function
transcription regulation
gene expression regulation
nonhuman
article
priority journal
Drug Descriptors:
*RNA
*immunoglobulin enhancer binding protein
***aptamer**
DNA
CAS REGISTRY NO.: (RNA) 63231-63-0; (DNA) 9007-49-2

L11 ANSWER 2 OF 17 EMBASE
on STN
ACCESSION NUMBER: 1998397104 EMBASE
TITLE: Anti-L-selectin oligonucleotide ligands recognize CD62L-positive leukocytes: Binding affinity and specificity of univalent and **bivalent** ligands.
AUTHOR: Ringquist S.; Parma D.
CORPORATE SOURCE: D. Parma, NeXstar Pharmaceuticals, Inc., 2860 Wilderness Place, Boulder, CO 80301, United States. parma@nexstar.com
SOURCE: Cytometry, (1 Dec 1998) Vol. 33, No. 4, pp. 394-405.
Refs: 81

ISSN: 0196-4763 CODEN: CYTODQ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19981217
Last Updated on STN: 19981217

ABSTRACT: Oligonucleotide **aptamers** generated against purified LS-Rg, a human L- selectin/IgG fusion protein, bound human CD62L-positive leukocytes. FACS analysis of lymphocytes or neutrophils stained with fluorescently labeled ***aptamers*** indicated specificity and sensitivity for cellular L-selectin similar to that observed with anti-L-selectin antibody. Univalent ***aptamers*** were compared to **bivalent aptamers** as well as to the anti-adhesion, anti-L- selectin antibody DREG56. Equilibrium and kinetic binding experiments were performed to examine the affinity and kinetic binding parameters of L- selectin **aptamers** to evaluate their binding to CD62L-positive leukocytes and to test their potential as L-selectin antagonists. Binding experiments indicated that **bivalent** ***aptamers*** approached the affinity and the dissociation rate of ***bivalent*** antibody, and preferentially recognized cellular compared to soluble L-selectin, a potentially useful distinction in vivo. Anti-L-selectin ***aptamers*** also inhibited L-selectin dependent self-adhesion of neutrophils suggesting that in vitro univalent and **bivalent** ***aptamers*** provided anti- adhesion activity similar to that observed with blocking antibody and indicated a direct blocking mechanism of action during inhibition of L- selectin-dependent trafficking of lymphocytes observed in vivo.

CONTROLLED TERM: Medical Descriptors:
*flow cytometry
*leukocyte adherence
ligand binding
antigen recognition
binding affinity
fluorescence microscopy
dissociation constant
neutrophil chemotaxis
lymphocyte subpopulation
human
controlled study
human cell
article
priority journal
Drug Descriptors:
*l selectin: EC, endogenous compound
*padgem protein
*hybrid protein: EC, endogenous compound
selectin antagonist
l selectin antibody
okt 8
monoclonal antibody cd11b
monoclonal antibody cd 20
okt 4
monoclonal antibody cd 62
unclassified drug
CAS REGISTRY NO.: (l selectin) 126880-86-2

L11 ANSWER 3 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:252273 BIOSIS

DOCUMENT NUMBER: PREV200300252273
TITLE: Yeast genetic selections to optimize RNA decoys for transcription factor NF-kappaB.
AUTHOR(S): Cassiday, Laura A.; Maher, L. James III [Reprint Author]
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Mayo Foundation, 200 First Street SW, Guggenheim 16, Rochester, MN, 55905, USA
maher@mayo.edu
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (April 1 2003) Vol. 100, No. 7, pp. 3930-3935. print.
ISSN: 0027-8424 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 May 2003
Last Updated on STN: 28 May 2003
ABSTRACT:In vitro-selected RNA **aptamers** are potential inhibitors of disease-related proteins. Our laboratory previously isolated an RNA ***aptamer*** that binds with high affinity to human transcription factor NF-kappaB. This RNA **aptamer** competitively inhibits DNA binding by NF-kappaB in vitro and is recognized by its target protein in vivo in a yeast three-hybrid system. In the present study, yeast genetic selections were used to optimize the RNA **aptamer** for binding to NF-kappaB in the eukaryotic nucleus. Selection for improved binding to NF-kappaB from RNA libraries encoding (i) degenerate **aptamer** variants and (ii) sequences present at round 8 of 14 total rounds of in vitro selection yielded RNA ***aptamers*** with dramatically improved in vivo activity. Furthermore, we show that an in vivo-optimized RNA **aptamer** exhibits specific "decoy" activity, inhibiting transcriptional activation by its NF-kappaB target protein in a yeast one-hybrid assay. This decoy activity is enhanced by the expression of a **bivalent aptamer**. The combination of in vitro and in vivo genetic selections was crucial for obtaining RNA **aptamers** with in vivo decoy activity.
CONCEPT CODE: Genetics - General 03502
Genetics - Plant 03504
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Pharmacology - General 22002
INDEX TERMS: Major Concepts
Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics); Pharmacology
INDEX TERMS: Parts, Structures, & Systems of Organisms
nucleus
INDEX TERMS: Chemicals & Biochemicals
DNA: transcription inhibition; NF-kappa-B [nuclear factor-kappa-B]; RNA: pharmaceutical
INDEX TERMS: Methods & Equipment
RNA engineering: laboratory techniques; genetic selection: genetic techniques, laboratory techniques; yeast one-hybrid assay: genetic techniques, laboratory techniques; yeast three-hybrid assay: genetic techniques, laboratory techniques
ORGANISM: Classifier
Fungi 15000
Super Taxa
Plantae
Organism Name
yeast (common)
Taxa Notes

L11 ANSWER 4 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:28644 BIOSIS
DOCUMENT NUMBER: PREV199900028644
TITLE: Anti-L-selectin oligonucleotide ligands recognize CD62L-positive leukocytes: Binding affinity and specificity of univalent and **bivalent** ligands.
AUTHOR(S): Ringquist, Steven; Parma, David [Reprint author]
CORPORATE SOURCE: NeXstar Pharmaceuticals Inc., 2860 Wilderness Place, Suite 200, Boulder, CO 80301, USA
SOURCE: Cytometry, (Dec. 1, 1998) Vol. 33, No. 4, pp. 394-405. print.
CODEN: CYTODQ. ISSN: 0196-4763.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Feb 1999
Last Updated on STN: 3 Feb 1999

ABSTRACT:Oligonucleotide **aptamers** generated against purified LS-Rg, a human L-selectin/IgG fusion protein, bound human CD62L positive leukocytes. FACS analysis of lymphocytes or neutrophils stained with fluorescently labeled ***aptamers*** indicated specificity and sensitivity for cellular L-selectin similar to that observed with anti-L-selectin antibody. Univalent ***aptamers*** were compared to **bivalent aptamers** as well as to the anti-adhesion, anti-selectin antibody DREG56. Equilibrium and kinetic binding experiments were performed to examine the affinity and kinetic binding parameters of L-selectin **aptamers** to evaluate their binding to CD62L-positive leukocytes and to test their potential as L-selectin antagonists. Binding experiments indicated that **bivalent** ***aptamers*** approached the affinity and the dissociation rate of ***bivalent*** antibody, and preferentially recognized cellular compared to soluble L-selectin, a potentially useful distinction in vivo. Anti-selectin ***aptamers*** also inhibited L-selectin dependent self-adhesion of neutrophils suggesting that in vitro univalent and **bivalent** ***aptamers*** provided anti-adhesion activity similar to that observed with blocking antibody and indicated a direct blocking mechanism of action during inhibition of L-selectin-dependent trafficking of lymphocytes observed in vivo.

CONCEPT CODE: Biophysics - Methods and techniques 10504
Cytology - Human 02508
Immunology - General and methods 34502
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064

INDEX TERMS: Major Concepts
Cell Biology; Methods and Techniques

INDEX TERMS: Parts, Structures, & Systems of Organisms
CD62L-positive leukocytes: blood and lymphatics, immune system

INDEX TERMS: Chemicals & Biochemicals
anti-L-selectin **aptamers**; anti-L-selectin oligonucleotide ligands; DREG56: anti-L-selectin antibody

INDEX TERMS: Methods & Equipment
flow cytometry: analytical method, cytophotometry: CT; neutrophil-neutrophil adhesion assay: Analysis/Characterization Techniques: CT, analytical method; nitrocellulose filter binding assay: analytical method, binding assays; FACSCalibur fluorescence activated cell sorter: equipment

ORGANISM: Classifier
Hominidae 86215

Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

REGISTRY NUMBER: 9004-70-0 (NITROCELLULOSE)

L11 ANSWER 5 OF 17 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:320652 SCISEARCH
THE GENUINE ARTICLE: 664JR
TITLE: Yeast genetic selections to optimize RNA decoys for transcription factor NF-kappa B
AUTHOR: Cassiday L A; Maher L J (Reprint)
CORPORATE SOURCE: Mayo Clin & Mayo Fdn, Dept Biochem & Mol Biol, 200 1st St SW, Guggenheim 16, Rochester, MN 55905 USA (Reprint); Mayo Clin & Mayo Fdn, Dept Biochem & Mol Biol, Rochester, MN 55905 USA
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1 APR 2003) Vol. 100, No. 7, pp. 3930-3935.
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418 USA.
ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 25
ABSTRACT:

In vitro-selected RNA **aptamers** are potential inhibitors of disease-related proteins. Our laboratory previously isolated an RNA ***aptamer*** that binds with high affinity to human transcription factor NF-kappaB. This RNA **aptamer** competitively inhibits DNA binding by NF-kappaB in vitro and is recognized by its target protein in vivo in a yeast three-hybrid system. In the present study, yeast genetic selections were used to optimize the RNA **aptamer** for binding to NF-kappaB in the eukaryotic nucleus. Selection for improved binding to NF-kappaB from RNA libraries encoding (f) degenerate **aptamer** variants and (6) sequences present at round 8 of 14 total rounds of in vitro selection yielded RNA ***aptamers*** with dramatically improved in vivo activity. Furthermore, we show that an in vivo-optimized RNA **aptamer** exhibits specific "decoy" activity, inhibiting transcriptional activation by its NF-kappaB target protein in a yeast one-hybrid assay. This decoy activity is enhanced by the expression of a **bivalent aptamer**. The combination of in vitro and in vivo genetic selections was crucial for obtaining RNA **aptamers** with in vivo decoy activity.

CATEGORY: MULTIDISCIPLINARY SCIENCES
SUPPL. TERM PLUS: SACCHAROMYCES-CEREVISIAE; IN-VIVO; FACTOR TARGET; **APTAMER**; DNA; INHIBITION; ACTIVATION; SITE

REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
*CLONTECH	1999		34	YEAST PROT HDB
BAEUERLE P A	1996	87	13	CELL
BEG A A	1996	274	782	SCIENCE
BLIND M	1999	96	3606	P NATL ACAD SCI USA
CAHIRMCFARLAND E D	2000	97	6055	P NATL ACAD SCI USA
CAPONIGRO G	1993	13	5141	MOL CELL BIOL

CASSIDAY L A	2002	30	4118	NUCLEIC ACIDS RES
CASSIDAY L A	2001	40	2433	BIOCHEMISTRY-US
CASSIDAY L A	2002	306	290	ANAL BIOCHEM
ERHART E	1983	156	625	J BACTERIOL
FUJITA T	1992	6	775	GENE DEV
GHOSH G	1995	373	303	NATURE
HANNON G J	2002	418	244	NATURE
ISHIZAKI J	1996	2	1386	NAT MED
JAEGER J A	1990	183	281	METHOD ENZYMOL
JAEGER J A	1989	86	7706	P NATL ACAD SCI USA
KUNSCH C	1992	12	4412	MOL CELL BIOL
LEBRUSKA L L	1999	38	3168	BIOCHEMISTRY-US
MARTELL R E	2002	6	30	MOL THER
MORISHITA R	1997	3	894	NAT MED
SENGUPTA D J	1996	93	8496	P NATL ACAD SCI USA
SHI H	1999	96	10033	P NATL ACAD SCI USA
SULLENGER B A	2002	418	252	NATURE
ZHANG X T	2001	276	47844	J BIOL CHEM
ZUKER M	1989	244	48	SCIENCE

L11 ANSWER 6 OF 17 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1998:904343 SCISEARCH
THE GENUINE ARTICLE: 141GR
TITLE: Anti-L-selectin oligonucleotide ligands recognize CD62L-positive leukocytes: Binding affinity and specificity of univalent and **bivalent** ligands
AUTHOR: Ringquist S; Parma D (Reprint)
CORPORATE SOURCE: NEXSTAR PHARMACEUT INC, 2860 WILDERNESS PL, SUITE 200, BOULDER, CO 80301 (Reprint); NEXSTAR PHARMACEUT INC, BOULDER, CO 80301
COUNTRY OF AUTHOR: USA
SOURCE: CYTOMETRY, (1 DEC 1998) Vol. 33, No. 4, pp. 394-405. Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012. ISSN: 0196-4763.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 81
ABSTRACT:

Oligonucleotide **aptamers** generated against purified LS-Rg, a human L-selectin/IgG fusion protein, bound human CD62L-positive leukocytes. FAGS analysis of lymphocytes or neutrophils stained with fluorescently labeled ***aptamers*** indicated specificity and sensitivity for cellular L-selectin similar to that observed with anti-L-selectin antibody. Univalent ***aptamers*** were compared to **bivalent aptamers** as well as to the anti-adhesion, anti-L-selectin antibody DREG56. Equilibrium and kinetic binding experiments were performed. to examine the affinity acid kinetic binding parameters of L-selectin **aptamers** to evaluate their binding to CD62L-positive leukocytes and to test their potential as L-selectin antagonists. Binding experiments indicated that **bivalent** ***aptamers*** approached the affinity and the dissociation rate of ***bivalent*** antibody, and preferentially recognized cellular compared to soluble L-selectin, a potentially useful distinction in vivo. Anti-L-selectin ***aptamers*** also inhibited L-selectin dependent self-adhesion of neutrophils suggesting that in vitro univalent and **bivalent** ***aptamers*** provided anti-adhesion activity similar to that observed with blocking antibody and indicated a direct blocking mechanism of action during inhibition of L-selectin-dependent trafficking of lymphocytes observed in vivo. (C) 1998 Wiley-Liss,Inc.

CATEGORY: CELL BIOLOGY; BIOCHEMICAL RESEARCH METHODS
SUPPLEMENTARY TERM: adhesion molecules; FAGS staining; cell-to-cell interactions; inflammation
SUPPL. TERM PLUS: NODE HOMING RECEPTOR; MEDIATED LUNG INJURY; Q-BETA REPLICASE; RNA LIGANDS; LYMPHOCYTE RECIRCULATION; MONOCLONAL-ANTIBODY; IN-VIVO; CD18-INDEPENDENT ADHESION; EXPONENTIAL ENRICHMENT; NEUTROPHIL AGGREGATION

REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
ARBONES M L	1994	1	247	IMMUNITY
BERTOZZI C R	1995	34	14271	BIOCHEMISTRY-US
BRADLEY L M	1994	180	2401	J EXP MED
BROWN D	1995	34	14765	BIOCHEMISTRY-US
BROWN D	1995	34	14775	BIOCHEMISTRY-US
BROWN D	1996	93	11558	P NATL ACAD SCI USA
BUTCHER E C	1996	272	60	SCIENCE
CIESIOLKA J	1995	1	538	RNA
CONNELL G J	1993	32	5497	BIOCHEMISTRY-US
CONNELL G J	1994	264	1137	SCIENCE
CROTHERS D M	1972	9	341	IMMUNOCHEMISTRY
DAILEY M O	1982	128	2134	J IMMUNOL
DAVIS K A	1996	24	702	NUCLEIC ACIDS RES
DELISI C	1981	18	507	MOL IMMUNOL
DELISI C	1980	13	201	Q REV BIOPHYS
DOWER S K	1981	20	6326	BIOCHEMISTRY-US
ELLINGTON A D	1990	346	818	NATURE
GALLATIN W M	1983	304	30	NATURE
GENG J G	1992	267	19846	J BIOL CHEM
GEOFFROY J S	1989	198	2463	J CELL BIOL
GOLD L	1995	64	763	ANNU REV BIOCHEM
GOLD L	1995	270	13581	J BIOL CHEM
HALE S P	1996	93	2755	P NATL ACAD SCI USA
HALLMANN R	1991	174	236	BIOCHEM BIOPH RES CO
HICKE B J	1996	98	2688	J CLIN INVEST
HOU S	1995	155	252	J IMMUNOL
ILLANGASEKARE M	1995	267	643	SCIENCE
IRVINE D	1991	222	739	J MOL BIOL
JAYASENA V K	1996	7	2349	BIOCHEMISTRY-US
JENISON R D	1994	263	1425	SCIENCE
JUNG T M	1988	141	4110	J IMMUNOL
JUTILA M A	1989	143	3318	J IMMUNOL
KANOF M E	1988	140	3701	J IMMUNOL
KANSAS G S	1993	177	833	J EXP MED
KANSAS G S	1985	134	2995	J IMMUNOL
KAUFMAN E N	1992	52	4157	CANCER RES
KISHIMOTO T K	1991	78	805	BLOOD
KISHIMOTO T K	1990	87	2244	P NATL ACAD SCI USA
KISHIMOTO T K	1989	245	1238	SCIENCE
KLOTZ I M	1985	18	227	Q REV BIOPHYS
LEWINSOHN D M	1987	138	4313	J IMMUNOL
LEY K	1991	77	2553	BLOOD
LEY K	1993	82	1632	BLOOD
LEY K	1995	181	669	J EXP MED
LEY K	1995	155	525	J IMMUNOL
LIPKIN E W	1986	261	1702	J BIOL CHEM
LUSCINSKAS F W	1994	125	1417	J CELL BIOL
MA X L	1993	88	649	CIRCULATION
MAYO K H	1989	264	17838	J BIOL CHEM
MIHELCIC D	1994	84	2322	BLOOD
MULLIGAN M S	1991	88	1396	J CLIN INVEST

MULLIGAN M S	1993	151	6410	J IMMUNOL
MULLIGAN M S	1994	152	832	J IMMUNOL
NAVARRO R F	1985	162	1075	J EXP MED
NIEUWLANDT D	1995	34	5651	BIOCHEMISTRY-US
NORGARD K E	1993	90	1068	P NATL ACAD SCI USA
OCONNELL D	1996	93	5883	P NATL ACAD SCI USA
PICKER L J	1993	150	1105	J IMMUNOL
POLLET R J	1977	252	5828	J BIOL CHEM
REICHERT R A	1983	157	813	J EXP MED
REYNOLDS J A	1979	18	264	BIOCHEMISTRY-US
RIGGS A D	1970	53	401	J MOL BIOL
RINGQUIST S	1993	32	10254	BIOCHEMISTRY-US
RINGQUIST S	1995	34	3640	BIOCHEMISTRY-US
SCHNEIDER D	1992	228	862	J MOL BIOL
SIMON S I	1993	82	1097	BLOOD
SIMON S I	1990	111	2747	J CELL BIOL
SIMON S I	1992	149	2765	J IMMUNOL
SPERTINI O	1991	5	300	LEUKEMIA
SPERTINI O	1991	349	691	NATURE
SPRINGER T A	1995	57	827	ANNU REV PHYSIOL
TEDDER T F	1995	9	866	FASEB J
TEDDER T F	1995	181	2259	J EXP MED
TEDDER T F	1990	144	532	J IMMUNOL
TUERK C	1990	249	505	SCIENCE
VONANDRIAN U H	1992	263	H1034	AM J PHYSIOL
VONANDRIAN U H	1993	91	2893	J CLIN INVEST
VONANDRIAN U H	1991	87	7538	P NATL ACAD SCI USA
WATSON S R	1991	349	164	NATURE
YARUS M	1969	42	171	J MOL BIOL
YEDNOCK T A	1987	104	725	J CELL BIOL

L11 ANSWER 7 OF 17 MEDLINE on STN

ACCESSION NUMBER: 2003155336 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12637683

TITLE: Yeast genetic selections to optimize RNA decoys for transcription factor NF-kappa B.

AUTHOR: Cassiday Laura A; Maher L James 3rd

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Mayo Foundation, Rochester, MN 55905, USA.

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2003 Apr 1) 100 (7) 3930-5. Electronic Publication: 2003-03-13. Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200305

ENTRY DATE: Entered STN: 20030403
Last Updated on STN: 20030523
Entered Medline: 20030522

ABSTRACT:
In vitro-selected RNA **aptamers** are potential inhibitors of disease-related proteins. Our laboratory previously isolated an RNA ***aptamer*** that binds with high affinity to human transcription factor NF-kappaB. This RNA **aptamer** competitively inhibits DNA binding by NF-kappaB in vitro and is recognized by its target protein in vivo in a yeast three-hybrid system. In the present study, yeast genetic selections were used to optimize the RNA **aptamer** for binding to NF-kappaB in the eukaryotic nucleus. Selection for improved binding to NF-kappaB from RNA libraries encoding (i) degenerate **aptamer** variants and (ii) sequences present at round 8 of 14 total rounds of in vitro selection yielded RNA

aptamers with dramatically improved in vivo activity. Furthermore, we show that an in vivo-optimized RNA **aptamer** exhibits specific "decoy" activity, inhibiting transcriptional activation by its NF-kappaB target protein in a yeast one-hybrid assay. This decoy activity is enhanced by the expression of a **bivalent aptamer**. The combination of in vitro and in vivo genetic selections was crucial for obtaining RNA **aptamers** with in vivo decoy activity.

CONTROLLED TERM: Base Sequence
Cloning, Molecular
Kinetics
Molecular Sequence Data
*NF-kappa B: ME, metabolism
Nucleic Acid Conformation
RNA, Fungal: CH, chemistry
*RNA, Fungal: GE, genetics
RNA, Fungal: ME, metabolism
Research Support, Non-U.S. Gov't
*Saccharomyces cerevisiae: GE, genetics
Saccharomyces cerevisiae Proteins: GE, genetics
*Selection (Genetics)

CHEMICAL NAME: 0 (NF-kappa B); 0 (RNA, Fungal); 0 (Saccharomyces cerevisiae Proteins)

L11 ANSWER 8 OF 17 MEDLINE on STN

ACCESSION NUMBER: 1999059566 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9845433

TITLE: Anti-L-selectin oligonucleotide ligands recognize CD62L-positive leukocytes: binding affinity and specificity of univalent and **bivalent** ligands.

AUTHOR: Ringquist S; Parma D

CORPORATE SOURCE: NeXstar Pharmaceuticals, Inc., Boulder, Colorado 80301, USA.

SOURCE: Cytometry : journal of the Society for Analytical Cytology, (1998 Dec 1) 33 (4) 394-405.
Journal code: 8102328. ISSN: 0196-4763.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199902

ENTRY DATE: Entered STN: 19990223
Last Updated on STN: 19990223
Entered Medline: 19990211

ABSTRACT:
Oligonucleotide **aptamers** generated against purified LS-Rg, a human L-selectin/IgG fusion protein, bound human CD62L-positive leukocytes. FACS analysis of lymphocytes or neutrophils stained with fluorescently labeled ***aptamers*** indicated specificity and sensitivity for cellular L-selectin similar to that observed with anti-L-selectin antibody. Univalent ***aptamers*** were compared to **bivalent aptamers** as well as to the anti-adhesion, anti-L-selectin antibody DREG56. Equilibrium and kinetic binding experiments were performed to examine the affinity and kinetic binding parameters of L-selectin **aptamers** to evaluate their binding to CD62L-positive leukocytes and to test their potential as L-selectin antagonists. Binding experiments indicated that **bivalent** ***aptamers*** approached the affinity and the dissociation rate of ***bivalent*** antibody, and preferentially recognized cellular compared to soluble L-selectin, a potentially useful distinction in vivo. Anti-L-selectin ***aptamers*** also inhibited L-selectin dependent self-adhesion of neutrophils suggesting that in vitro univalent and **bivalent** ***aptamers*** provided anti-adhesion activity similar to that observed with blocking antibody and indicated a direct blocking mechanism of action during

inhibition of L-selectin-dependent trafficking of lymphocytes observed in vivo.
CONTROLLED TERM: Base Sequence
Cell Adhesion
Humans
Kinetics
*L-Selectin: AN, analysis
L-Selectin: IM, immunology
*Leukocytes: IM, immunology
Ligands
Lymphocytes: IM, immunology
Molecular Sequence Data
Neutrophils: IM, immunology
Neutrophils: ME, metabolism
*Oligonucleotides: IM, immunology
Solubility
Staining and Labeling
CAS REGISTRY NO.: 126880-86-2 (L-Selectin)
CHEMICAL NAME: 0 (Ligands); 0 (Oligonucleotides)

L11 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:48600 CAPLUS
DOCUMENT NUMBER: 142:312421
ENTRY DATE: Entered STN: 20 Jan 2005
TITLE: Nucleic Acid-Based Fluorescence Sensors for Detecting Proteins
AUTHOR(S): Heyduk, Ewa; Heyduk, Tomasz
CORPORATE SOURCE: Edward A. Doisy Department of Biochemistry and Molecular Biology, St. Louis University Medical School, St. Louis, MO, 63104, USA
SOURCE: Analytical Chemistry (2005), 77(4), 1147-1156
CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 9-5 (Biochemical Methods)
Section cross-reference(s): 3

ABSTRACT:
We report here development of a rapid, homogeneous, **aptamer**-based fluorescence assay ("mol. beacons") for detecting proteins. The assay involves protein-induced coassocn. of two **aptamers** recognizing two distinct epitopes of the protein. The **aptamers** contain short fluorophore-labeled complementary "signaling" oligonucleotides attached to the ***aptamer*** by non-DNA linker. Coassocn. of the two **aptamers** with the protein results in bringing the two "signaling" oligonucleotides into proximity, producing a large change of fluorescence resonance energy transfer between the fluorophores. We used thrombin as a model system to provide proof-of-principle evidence validating this mol. beacon design. Thrombin beacon was capable of detecting the protein with high selectivity (also in complex biol. mixts.), picomolar sensitivity, and high signal-to-background ratio. This is a homogeneous assay requiring no sample manipulation. Since the design of mol. beacons described here is not limited to any specific protein, it will be possible to develop these beacons to detect a variety of target proteins of biomedical importance.

SUPPL. TERM: **aptamer** beacon FRET detection protein thrombin model; fluorescence resonance energy transfer detection protein
INDEX TERM: Proteins
ROLE: ANT (Analyte); ANST (Analytical study)
(DNA-binding; nucleic acid-based fluorescence sensors for detecting proteins)
INDEX TERM: Oligonucleotides

ROLE: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(attached to the **aptamer** by non-DNA linker; nucleic acid-based fluorescence sensors for detecting proteins)

INDEX TERM: **Aptamers**
(**bivalent** thrombin, attached to oligonucleotides by non-DNA linker; nucleic acid-based fluorescence sensors for detecting proteins)

INDEX TERM: Biosensors
Electrophoresis
Fluorescence
Fluorescence resonance energy transfer
Fluorometry
(nucleic acid-based fluorescence sensors for detecting proteins)

INDEX TERM: 2321-07-5, Fluorescein 6268-49-1, Dabcyl 82354-19-6, Texas Red 146368-14-1, Cy5
ROLE: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleic acid-based fluorescence sensors for detecting proteins)

INDEX TERM: 9002-04-4, Thrombin
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(nucleic acid-based fluorescence sensors for detecting proteins)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

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L11 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1080626 CAPLUS

DOCUMENT NUMBER: 142:49205
ENTRY DATE: Entered STN: 17 Dec 2004
TITLE: Stabilized **aptamers** to growth factors and their receptors for use in the treatment of solid tumors
INVENTOR(S): Epstein, David; Grate, Dilara; Stanton, Martin; Diener, John L.; Wilson, Charles; McCauley, Thomas; DeSouza, Errol
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 96 pp., Cont.-in-part of U.S. Ser. No. 762,915.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07H021-04
SECONDARY: C07K014-705
US PATENT CLASSIF.: 435069100; 435320100; 435325000; 530350000; 536023200
CLASSIFICATION: 1-6 (Pharmacology)
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004253679	A1	20041216	US 2004-829504		20040421
US 2004180360	A1	20040916	US 2003-718833		20031121
US 2004253243	A1	20041216	US 2004-762915		20040121
PRIORITY APPLN. INFO.:			US 2002-428102P	P	20021121
			US 2003-441357P	P	20030121
			US 2003-463095P	P	20030415
			US 2003-464179P	P	20030421
			US 2003-464239P	P	20030421
			US 2003-465053P	P	20030423
			US 2003-465055P	P	20030423
			US 2003-469628P	P	20030508
			US 2003-474133P	P	20030529
			US 2003-474680P	P	20030529
			US 2003-486580P	P	20030711
			US 2003-489810P	P	20030723
			US 2003-491019P	P	20030729
			US 2003-503596P	P	20030916
			US 2003-512071P	P	20031017
			US 2003-718833	A2	20031121
			US 2004-537045P	P	20040116
			US 2004-537201P	P	20040116
			US 2004-762915	A2	20040121

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004253679	ICM	C07H021-04
	ICS	C07K014-705
	INCL	435069100; 435320100; 435325000; 530350000; 536023200
US 2004253679	NCL	435/069.100; 435/320.100; 435/325.000; 530/350.000; 536/023.200
US 2004180360	NCL	435/006.000; 536/023.500
US 2004253243	NCL	424/145.100

ABSTRACT:
Aptamers that bind specifically to platelet-derived growth factor, vascular endothelial growth factor, their receptors and isoforms of the growth factors are described for use in the treatment of solid tumors dependent on these growth factors. They can be used alone or in combination with known cytotoxic agents for the treatment of solid tumors. The **aptamers** are

modified, e.g. by using modified backbones or conjugation with polyethylene glycol, to improve in vivo stability. **Aptamers** with one or more immunostimulant CpG motifs are also described. **Bivalent** ***aptamers*** binding one of these targets and another growth- or apoptosis-regulating are also described.

SUPPL. TERM: PDGF VEGF receptor **aptamer** solid tumor cytotoxin therapy

INDEX TERM: Platelet-derived growth factors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(AA; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Platelet-derived growth factors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(AB; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: CD80 (antigen)
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(B7-X, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Cytokines
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(BAFF, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Platelet-derived growth factors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(BB; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(BTLA (B7x receptors), **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Platelet-derived growth factors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(CC and DD isoforms; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: CD antigens
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(CD11C, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: CD antigens
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(CD33, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Immunostimulants
(CpG dinucleotide as, in **aptamers**; stabilized **aptamers** to growth factors and their receptors

for use in treatment of solid tumors)

INDEX TERM: Immunoglobulin receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(IgE type I, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Immunoglobulin receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(IgE type IIb, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Antibodies and Immunoglobulins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(IgE, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(PD-L1 (programmed death ligand 1), **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(PDCD (programmed cell death), PD-1, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Antigens
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(PSMA (prostate-specific membrane antigen), **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Genetic methods
(SELEX, for selection of **aptamers**; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(TIM-3 (T cell Ig- and mucin-domain- containing mol.-3), **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(TLR (Toll-like receptor), **aptamers** binding growth factors and their receptors and; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Cytotoxic agents
(antimetabolites, cancer therapy with **aptamers** and; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: CD19 (antigen)
CD20 (antigen)

CD22 (antigen)
CTLA-4 (antigen)
Tumor necrosis factors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(**aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Alkylating agents, biological
Angiogenesis inhibitors
(cancer therapy with **aptamers** and; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Nucleoside analogs
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer therapy with **aptamers** and; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Tubulins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(cytotoxins acting on, cancer therapy with **aptamers** and; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Toxins
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytotoxins, cancer therapy with **aptamers** and; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Sarcoma
(fibrosarcoma, dermafibrosarcoma protruberans, therapy with **aptamers** and cytotoxins; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Neuroglia, neoplasm
(glioblastoma, therapy with **aptamers** and cytotoxins; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Oligonucleotides
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunostimulatory, **aptamers** containing; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Leukemia
(myelomonocytic, chronic, therapy with **aptamers** and cytotoxins; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Animal tissue, disease
(soft, neoplasm, sarcoma, therapy with **aptamers** and cytotoxins; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Sarcoma
(soft-tissue, therapy with **aptamers** and cytotoxins; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid

tumors)

INDEX TERM: Antitumor agents
Aptamers
(stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Platelet-derived growth factor receptors
Vascular endothelial growth factor receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Digestive tract, neoplasm
(stroma, therapy with **aptamers** and cytotoxins; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Interleukin 2 receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(α chain, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: Integrins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(αX, **aptamers** for; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: 2382-65-2D, **aptamers** containing
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as immunostimulant; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: 51-21-8, 5-Fluorouracil 59-05-2, Methotrexate 147-94-4, Cytarabine 865-21-4, Vinblastin 15663-27-1, Cisplatin 20830-81-3, Daunorubicin 23214-92-8, Doxorubicin 33069-62-4, Taxol 41575-94-4, Carboplatin 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 113440-58-7, Calicheamicin 114977-28-5, Docetaxel 152044-54-7, Epothilone B 189453-10-9, Epothilone D
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer therapy with **aptamers** and; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM:

808128-36-1	808197-55-9	808197-56-0	808197-57-1
808197-58-2	808197-59-3	808197-60-6	808197-61-7
808200-05-7	808200-06-8	808200-07-9	808200-08-0
808200-09-1	808200-10-4	808200-11-5	808200-12-6
808200-13-7	808200-14-8	808200-15-9	808200-16-0
808200-17-1	808200-18-2	808200-19-3	808200-20-6
808200-21-7	808200-22-8	808200-23-9	808200-24-0
808200-25-1	808200-26-2	808200-27-3	808200-28-4
808200-29-5	808200-30-8	808200-31-9	808200-32-0
808200-33-1	808200-34-2	808200-35-3	808200-36-4
808200-37-5	808200-38-6	808200-39-7	808200-40-0
808200-41-1	808793-77-3	808793-78-4	808793-79-5
808793-80-8	808793-81-9	808793-82-0	808793-83-1
808793-84-2	808793-85-3	808793-86-4	808793-87-5
808793-88-6	808793-89-7	808793-90-0	808793-91-1
808793-92-2	808793-93-3	808793-94-4	808793-95-5
808793-96-6	808793-97-7	808793-98-8	808793-99-9

808794-00-5 809292-29-3 809292-30-6
ROLE: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence, **aptamer** for platelet-derived growth factor; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: 120-73-0D, 1H-Purine, derivs.
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(purines, inhibitors of synthesis of, cancer therapy with **aptamers** and; stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: 127464-60-2, Vascular endothelial growth factor
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(stabilized **aptamers** to growth factors and their receptors for use in treatment of solid tumors)

INDEX TERM: 808200-49-9 808200-50-2 808200-51-3 808200-52-4
808200-53-5 808200-54-6 808200-55-7 808200-56-8
808200-57-9 808200-58-0
ROLE: PRP (Properties)
(unclaimed nucleotide sequence; stabilized **aptamers** to growth factors and their receptors for use in the treatment of solid tumors)

L11 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:70006 CAPLUS
DOCUMENT NUMBER: 140:123646
ENTRY DATE: Entered STN: 28 Jan 2004
TITLE: Method of screening for **bivalent** binding nucleic acid ligands (**aptamers**) of 7 transmembrane G protein-coupled receptors for therapeutic and diagnostic use
INVENTOR(S): Gold, Larry
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: U.S., 17 pp., Cont.-in-part of U.S. Ser. No. 956,699.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C12Q001-68
SECONDARY: C12P019-34
US PATENT CLASSIF.: 435006000; 435091200; 935077000; 935078000; 536023100; 536025400
CLASSIFICATION: 3-1 (Biochemical Genetics)
Section cross-reference(s): 2, 9, 63
FAMILY ACC. NUM. COUNT: 127
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6682886	B1	20040127	US 1998-118525	19980717
US 5683867	A	19971104	US 1994-234997	19940428
US 6083696	A	20000704	US 1997-956699	19971023
WO 2000004184	A1	20000127	WO 1999-US14853	19990630

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,

TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9947287	A1	20000207	AU 1999-47287		19990630
EP 1100960	A1	20010523	EP 1999-930840		19990630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AU 773741	B2	20040603	AU 2001-18257		20010202
AU 773815	B2	20040610	AU 2001-29834		20010323
US 2004091931	A1	20040513	US 2003-729667		20031205
PRIORITY APPLN. INFO.:			US 1994-234997	A1	19940428
			US 1997-956699	A2	19971023
			US 1990-536428	B2	19900611
			AU 1991-82061	A0	19910610
			US 1991-714131	A2	19910610
			US 1993-117991	B2	19930908
			US 1993-123935	B2	19930917
			US 1994-199507	A2	19940222
			US 1994-234797	A2	19940428
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PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6682886	ICM	C12Q001-68
	ICS	C12P019-34
	INCL	435006000; 435091200; 935077000; 935078000; 536023100; 536025400
US 6682886	NCL	435/006.000; 435/091.200; 536/023.100; 536/025.400
US 5683867	NCL	435/006.000; 435/091.200; 536/023.100; 536/025.400
	ECLA	C07H019/06E; C07H019/10E; C07H021/00C2; C07H021/00C4; C12N015/10C4; C12N015/11D; C12Q001/68A8+525/101; C12Q001/68A8; G01N033/532; G01N033/535; G01N033/68; G01N033/76
US 6083696	NCL	435/006.000; 435/091.200; 536/023.100; 536/024.300; 536/025.400
WO 2000004184	ECLA	C12Q001/68A8
US 2004091931	NCL	435/006.000; 435/007.100; 435/069.100; 435/320.100; 435/325.000; 530/350.000; 525/054.100; 530/395.000

ABSTRACT:
Methods for identifying and preparing **bivalent** binding mols. to 7 transmembrane domain containing G protein-coupled receptors, that can activate or inhibit 7 transmembrane G protein-coupled receptors, are described. SELEX (Systematic Evolution of Ligands by EXponential enrichment) method is used to screening high affinity nucleic acid ligands, also termed **aptamers**. It combines two or more binding domains to two or more different epitopes of the same 7 transmembrane G protein-coupled receptor. These SELEX-derived ***bivalent*** binding mols. comprise two or more binding domains which bind simultaneously to two or more epitopes of the same 7TM G protein-coupled receptor, thus has increased binding affinity to 7TM G protein-coupled receptor for their activation or inhibition. The method was exemplified by screening random RNA libraries for binding mols. to both ECL1 (extracellular loop 1) or ECL2 of neurokinin receptor NK1R using peptide affinity columns. The ***bivalent*** ligands, derived from two ECL1- and ECL1-binding RNA libraries by linking them through overlap-extension PCR reaction, can be enriched after cycles of SELEX process to generate double-stranded DNA templates for their future synthesis. These **bivalent** binding mols. may be useful as therapeutic and diagnostic agents.

SUPPL. TERM: drug screening **bivalent aptamer** 7TM G protein coupled receptor

INDEX TERM: Neurotensin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A, of human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Parathyroid hormone receptors
Secretin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A, of rat/opossum, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adenosine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A1, of rat or human or canine, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adenosine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A2B, of rat or human or sheep, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adenosine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A3, of human or sheep, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Bradykinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(B2, of human/rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Cholecystokinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(CCKA, of human/rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Cholecystokinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(CCKB, of canine or human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of

screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D1, of rat or human or rhesus, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D1A, of rat or human or rhesus, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D2, of rat or human or mouse, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D3, of rat or human, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D4, of human, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D5, of rat or human, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(GP2-7 or 5A or 5A(S12) or 5B, of mouse/human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Histamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(H1, of bovine, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7

transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Histamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(H2, of rat or canine or human, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M1, of mouse or human, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M2, of human, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M3, of human, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M4, of human or chicken, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M5, of human/rat, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Oligonucleotides
ROLE: BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(RNA **aptamers**, binding to G protein coupled-receptor epitopes; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Genetic methods
(SELEX; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR1, of rat/human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers**

of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR2, of mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR3, of rat/human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR4, of human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR5, of human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Polysiloxanes, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(amino, **aptamers** linked by; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Angiotensin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(angiotensin II, of human/rat/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Liposomes
(**aptamers** linked by; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Hydrocarbons, biological studies
Monosaccharides
Oligosaccharides, biological studies
Peptides, biological studies
Polynucleotides
Polyoxyalkylenes, biological studies
Proteins
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**aptamers** linked by; method of screening for

bivalent binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Polysiloxanes, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hydroxy, **aptamers** linked by; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: DNA
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(linker, for generation of **bivalent** RNA ligands to G protein-coupled receptors epitopes; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Canis familiaris
Human
Mus
Rattus
(method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: G protein-coupled receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Epitopes
(of G protein-coupled receptors; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Thyrotropin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of canine/rat or human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Gonadotropin-releasing hormone receptor
VIP receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Gonadotropin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of human/rat/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Calcitonin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of human/rat/pig, screening for **bivalent**

nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Corticotropin releasing factor receptors
Glucagon receptors
Growth hormone-releasing hormone receptors
Neuropeptide Y receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of swine or Drosophila, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Affinity chromatography
(screening for **bivalent** ligand to G protein-coupled receptors epitopes; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Polysiloxanes, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(thio or carboxy-functionalized, **aptamers** linked by; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: PCR (polymerase chain reaction)
(to link G protein coupled receptor epitope ECL1- or ECL2-binding RNA mols.; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT1, 1C, of mouse/human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT1, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT1A, of rat/human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT1B, of rat/human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT1D, of canine/human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT1E, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT2, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT2B, of human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT3, of mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type 5-HT7, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Endothelin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type ETB, of human, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers**

of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Tachykinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type NK1, of human/mouse/rat, screening for **bivalent** nuclear acid ligands binding to peptides of; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Opioid receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(κ-opioid, of human/rat/mouse, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α1, of hamster or bovine, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α1D, of rat, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2, of human or mouse or fish, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2, of human or rat, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2A, of human or porcine or rat, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2B, of human or rat, screening for **bivalent** nuclear acid ligands binding to; method

of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2C, of mouse or rat, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(β1, of rat or human or mouse, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(β2, of rat or human or mouse, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(β3, of rat or human or bovine, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Opioid receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(δ-opioid, of human/mouse, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: Opioid receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(μ-opioid, of human/rat, screening for **bivalent** nuclear acid ligands binding to; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 9002-89-5, Ethenol, homopolymer 9003-01-4, 2-Propenoic acid homopolymer 9004-53-9, Dextrin 12619-70-4, Cyclodextrin 25322-68-3, Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy- 25322-69-4, Poly[oxy(methyl-1,2-ethanediyl)], α-hydro-ω-hydroxy-
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**aptamers** linked by; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 268720-50-9P, RNA (synthetic)
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(as ligands to G protein coupled-receptor; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 255916-21-3, L-Phenylalanine, L-histidyl-L-asparaginyl-L-α-glutamyl-L-tryptophyl-L-tyrosyl-L-tyrosylglycyl-L-leucyl-L-phenylalanyl-L-tyrosyl-L-cysteinyl-L-lysyl-
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(neurokinin receptor 1 extracellular loop 1; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

INDEX TERM: 255916-22-4, L-Valine, L-threonyl-L-threonyl-L-α-glutamyl-L-threonyl-L-methionyl-L-prolyl-L-seryl-L-arginyl-L-valyl-L-valyl-L-cysteinyl-L-methionyl-L-isoleucyl-L-α-glutamyl-L-tryptophyl-L-prolyl-L-α-glutamyl-L-histidyl-L-prolyl-L-asparaginyl-L-lysyl-L-isoleucyl-L-tyrosyl-L-α-glutamyl-L-lysyl-
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(neurokinin receptor 1 extracellular loop 2; method of screening for **bivalent** binding **aptamers** of 7 transmembrane GPCRs for therapeutic and diagnostic use)

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L11 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:290966 CAPLUS
DOCUMENT NUMBER: 139:18071
ENTRY DATE: Entered STN: 16 Apr 2003
TITLE: Yeast genetic selections to optimize RNA decoys for transcription factor NF-κB
AUTHOR(S): Cassiday, Laura A.; Maher, L. James, III
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Mayo Foundation, Rochester, MN, 55905, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(7), 3930-3935
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 3-2 (Biochemical Genetics)
Section cross-reference(s): 6

ABSTRACT:
In vitro-selected RNA **aptamers** are potential inhibitors of disease-related proteins. The laboratory previously isolated an RNA **aptamer** that binds with high affinity to human transcription factor NF-κB. This RNA **aptamer** competitively inhibits DNA binding by NF-κB in vitro and is recognized by its target protein in vivo in a yeast three-hybrid system. In the present study, yeast genetic selections were used to optimize the RNA **aptamer** for binding to NF-κB in the eukaryotic nucleus. Selection for improved binding to NF-κB from RNA libraries encoding (i) degenerate **aptamer** variants and (ii) sequences present at round 8 of 14 total rounds of in vitro selection yielded RNA **aptamers** with dramatically improved in vivo activity. Furthermore, the authors show that an in vivo-optimized RNA **aptamer** exhibits specific "decoy" activity, inhibiting transcriptional activation by its NF-κB target protein in a yeast one-hybrid assay. This decoy activity is enhanced by the expression of a ***bivalent*** **aptamer**. The combination of in vitro and in vivo genetic selections was crucial for obtaining RNA **aptamers** with in vivo decoy activity.

SUPPL. TERM: RNA **aptamer** transcription factor NFkappaB yeast selection

INDEX TERM: Transcription factors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(NF-κB (nuclear factor of κ light chain gene enhancer in B-cells); yeast three hybrid system to optimize α-p50 RNA **aptamer** binding to human transcription factor NF-κB)

INDEX TERM: **Aptamers**
Combinatorial library
(RNA; yeast three hybrid system to optimize α-p50 RNA **aptamer** binding to human transcription factor NF-κB)

INDEX TERM: Post-transcriptional processing
(interference; yeast three hybrid system to optimize α-p50 RNA **aptamer** binding to human transcription factor NF-κB)

INDEX TERM: Genetic selection
Human
Molecular association
Yeast
(yeast three hybrid system to optimize α-p50 RNA **aptamer** binding to human transcription factor NF-κB)

INDEX TERM: 539023-00-2 539023-01-3 539023-02-4 539023-03-5
539023-04-6 539023-05-7 539023-06-8
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(RNA **aptamer**; yeast three hybrid system to optimize α-p50 RNA **aptamer** binding to human transcription factor NF-κB)

INDEX TERM: 539023-07-9
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(yeast three hybrid system to optimize α-p50 RNA **aptamer** binding to human transcription factor NF-κB)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

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L11 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:595004 CAPLUS
DOCUMENT NUMBER: 137:151578
ENTRY DATE: Entered STN: 09 Aug 2002
TITLE: High affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands
INVENTOR(S): Tahiri-Alaoui, Abdessamad; James, William S.
PATENT ASSIGNEE(S): Isis Innovation Limited, UK
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C12N015-11
SECONDARY: C07H021-00; C12Q001-68
CLASSIFICATION: 6-2 (General Biochemistry)
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002061079	A2	20020808	WO 2002-GB364	20020129
WO 2002061079	A3	20030904		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

GB 2001-2270	A	20010129
GB 2001-2271	A	20010129
GB 2001-2272	A	20010129
GB 2001-2273	A	20010129

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002061079	ICM	C12N015-11
	ICS	C07H021-00; C12Q001-68

ABSTRACT:
The present invention provides biligands which comprise at least two ***aptamers.*** In particular, a system for binding two **aptamers** together to provide **bivalent** or bispecific ligands is provided. The authors have isolated 2'-Fluoro-substituted RNA **aptamers** that bind to streptavidin (SA) with an affinity around 7 ± 1.8 nM, comparable with that of recently described peptide **aptamers**. Binding to SA was not prevented by prior saturation with biotin, enabling nucleic acid **aptamers** to form useful ternary complexes. Mutagenesis, secondary structure anal., RNase footprinting and deletion anal. provided evidence for the essential structural features of SA-binding **aptamers**. In order to provide a general method for the exploitation of these **aptamers**, the authors produced derivs. in which they were fused to the naturally structured RNA elements, CopT or CopA. In parallel, the authors produced derivs. of CD4-binding **aptamers** fused to the complementary CopA or CopT elements. When mixed, these two chimeric **aptamers** rapidly hybridized, by virtue of CopA-CopT complementarity, to form stable, bi-functional **aptamers** that the authors called "adaptamers". The authors show that a CD4-SA-binding adaptamer can be used to capture CD4 onto a SA-derivatized surface, illustrating their general utility as indirect affinity ligands.

SUPPL. TERM: RNA streptavidin **aptamer** CD4 antigen CopA CopT fusion ligand

INDEX TERM: RNA
ROLE: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(2'-Fluoro-substituted, as **aptamers**; high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: Nucleic acids
ROLE: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(analogs, 2'-Fluoro-substituted, as **aptamers**; high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: CD4 (antigen)
ROLE: BSU (Biological study, unclassified); BIOL (Biological

study)
(**aptamer** binding to; high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: Plasmids
(copA and copT, use in **aptamers**; high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: Gene, microbial
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(copA, use in **aptamers**; high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: Gene, microbial
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(copT, use in **aptamers**; high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: Envelope proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(gp120env, **aptamer** binding to; high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: rRNA sequences
(high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: Ligands
Nucleic acids
ROLE: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: 9013-20-1, Streptavidin
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(**aptamer** binding to; high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: 445359-28-4, RNA (synthetic RNA **aptamer** J58copA)
445359-29-5, RNA (synthetic RNA **aptamer** L45copT)
ROLE: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

INDEX TERM: 445361-54-6 445361-55-7 445361-56-8 445361-57-9
445361-58-0 445361-59-1 445361-60-4 445361-61-5
ROLE: PRP (Properties)
(unclaimed sequence; high affinity nucleic acid **aptamers** incorporated into bi-specific capture ligands)

L11 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:200806 CAPLUS
DOCUMENT NUMBER: 136:336715
ENTRY DATE: Entered STN: 19 Mar 2002
TITLE: Forced engagement of a RNA/protein complex by a chemical inducer of dimerization to modulate gene expression

AUTHOR(S): Harvey, Isabelle; Garneau, Philippe; Pelletier, Jerry
CORPORATE SOURCE: Department of Biochemistry, McGill University, Montreal, QC, H3G 1Y6, Can.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(4), 1882-1887
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 6-1 (General Biochemistry)
ABSTRACT:
A general strategy is described for forcing the engagement of an RNA/protein complex by using small-mol. ligands. A **bivalent** mol. was created by linking a protein-binding ligand to an RNA-binding ligand. On presentation of the chemical inducer of dimerization to the RNA by the protein, cooperative binding ensued, resulting in higher-affinity complexes. When the chemical inducer of dimerization was used to target the protein to an mRNA template, the resulting RNA/protein complex was sufficiently stable to inhibit mRNA translation. This approach provides a logic to modulate gene expression by using small-mol. ligands to recruit protein surfaces to mRNAs.

SUPPL. TERM: translation inhibition artificial RNA protein complex
INDEX TERM: Ribosome
(80 S; inhibition of initiation complex formation by a forced engagement of a RNA/protein complex streptavidin)
INDEX TERM: RNA
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(**aptamers** J6f1, XI; translation inhibition by an artificial RNA-protein complex)
INDEX TERM: Molecular association
Translation initiation
(translation inhibition by an artificial RNA-protein complex)
INDEX TERM: 9013-20-1, Streptavidin
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(inhibition of initiation complex formation by a forced engagement of a RNA/protein complex streptavidin)
INDEX TERM: 419573-18-5 419573-19-6 419573-20-9
ROLE: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(translation inhibition by an artificial RNA-protein complex)
INDEX TERM: 58-85-5D, Biotin, derivs. 32986-56-4D, Tobramycin, derivs.
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(translation inhibition by an artificial RNA-protein complex)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD.
REFERENCE(S):
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L11 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:68592 CAPLUS
DOCUMENT NUMBER: 132:105019
ENTRY DATE: Entered STN: 28 Jan 2000
TITLE: Synthesis and identification of **bivalent** binding RNA molecules to G protein-coupled receptors
INVENTOR(S): Gold, Larry
PATENT ASSIGNEE(S): Nexstar Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C12Q001-68
SECONDARY: C12P019-34
CLASSIFICATION: 9-14 (Biochemical Methods)
Section cross-reference(s): 1, 2, 3
FAMILY ACC. NUM. COUNT: 127
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004184	A1	20000127	WO 1999-US14853	19990630
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6682886	B1	20040127	US 1998-118525	19980717
AU 9947287	A1	20000207	AU 1999-47287	19990630
EP 1100960	A1	20010523	EP 1999-930840	19990630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI

AU 773741	B2	20040603	AU 2001-18257		20010202
AU 773815	B2	20040610	AU 2001-29834		20010323
PRIORITY APPLN. INFO.:			US 1998-118525	A	19980717
			AU 1991-82061	A0	19910610
			US 1994-234997	A1	19940428
			AU 1996-58839	A3	19960530
			AU 1996-61611	A3	19960604
			US 1997-956699	A2	19971023
			WO 1999-US14853	W	19990630

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000004184	ICM	C12Q001-68
	ICS	C12P019-34
WO 2000004184	ECLA	C12Q001/68A8
US 6682886	NCL	435/006.000; 435/091.200; 536/023.100; 536/025.400

ABSTRACT:
Methods for identifying and preparing **bivalent** binding mols. to 7 transmembrane domain containing G protein-coupled receptors are described. The methods are based on the SELEX method (Systematic Evolution of Ligands by EXponential enrichment) for generating high affinity nucleic acid ligands, termed **aptamers**. It combines two or more binding domains to two or more different epitopes of the same 7 transmembrane G protein-coupled receptor. The method was exemplified by screening in the random RNA library for binding mols. to either ECL1 (extracellular loop 1) or ECL2 of neurokinin receptor NK1R using peptide affinity columns. The **bivalent** ligands, derived from two ECL1- and ECL1-binding RNA libraries by linking them through overlap-extension PCR reaction, can be enriched after cycles of SELEX process to generate double-stranded DNA templates for their future synthesis . These ***bivalent*** binding mols. may be useful as therapeutic and diagnostic agents.

SUPPL. TERM: biosynthesis screening **bivalent** binding mol G protein coupled receptor; **aptamers** **bivalent** substance P receptor NK1R SELEX

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1, 1C, of mouse/human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1A, of rat/human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1B, of rat/human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides

of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1D, of canine/human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1E, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT2, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT2B, of human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT3, of mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT7, of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Neurotensin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A, of human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Parathyroid hormone receptors
Secretin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A, of rat/opossum, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adenosine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(A1, of rat or human or canine, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adenosine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A2B, of rat or human or sheep, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adenosine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(A3, of human or sheep, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Bradykinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(B2, of human/rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D1, of rat or human or rhesus, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D2, of rat or human or mouse, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D3, of rat or human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D4, of human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Dopamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(D5, of rat or human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Endothelin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological

study); USES (Uses)
(ETB, of human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 5-HT receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(GP2-7 or 5A or 5A(S12) or 5B, of mouse/human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Histamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(H1, of bovine, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Histamine receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(H2, of rat or canine or human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M1, of mouse or human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M2, of human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M3, of human, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M4, of human or chicken, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(M5, of human/rat, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Tachykinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(NK1, of human/mouse/rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Oligonucleotides
ROLE: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(RNA **aptamers**, binding to G protein coupled-receptor epitopes; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Genetic methods
(SELEX; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR1, of rat/human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR2, of mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR3, of rat/human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR4, of human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Somatostatin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SSTR5, of human/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Polysiloxanes, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(amino, **aptamers** linked by; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Angiotensin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological

study); USES (Uses)
(angiotensin II, of human/rat/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Liposomes
(**aptamers** linked by; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Hydrocarbons, biological studies
Monosaccharides
Oligosaccharides, biological studies
Peptides, biological studies
Polynucleotides
Polyoxyalkylenes, biological studies
Proteins, general, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**aptamers** linked by; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Cholecystokinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cholecystokinin A, of human/rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Cholecystokinin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cholecystokinin B, of canine or human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Polysiloxanes, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hydroxy, **aptamers** linked by; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: DNA
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(linker, for generation of **bivalent** RNA ligands to G protein-coupled receptors epitopes; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Epitopes
(of G protein-coupled receptors; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Thyrotropin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of canine/rat or human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Gonadotropin-releasing hormone receptor
VIP receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological

study); USES (Uses)
(of human, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Gonadotropin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of human/rat/mouse, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Calcitonin receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of human/rat/pig, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Corticotropin releasing factor receptors
Glucagon receptors
Growth hormone-releasing hormone receptors
Neuropeptide Y receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of rat, screening for **bivalent** nuclear acid ligands binding to peptides of; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Muscarinic receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of swine or Drosophila, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Affinity chromatography
(screening for **bivalent** ligand to G protein-coupled receptors epitopes; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: G protein-coupled receptors
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Polysiloxanes, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(thio or carboxy-functionalized, **aptamers** linked by; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: PCR (polymerase chain reaction)
(to link G protein coupled receptor epitope ECL1- or ECL2-binding RNA mols.; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Opioid receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(κ-opioid, of human/rat/mouse, screening for

bivalent nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α1, of hamster or bovine, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α1D, of rat, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2, D, of human or rat, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2, of human or mouse or fish, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2A, of human or porcine or rat, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2B, of human or rat, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(α2C, of mouse or rat, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(β1, of rat or human or mouse, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(β2, of rat or human or mouse, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Adrenoceptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(β3, of rat or human or bovine, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Opioid receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(δ-opioid, of human/mouse, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: Opioid receptors
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(μ-opioid, of human/rat, screening for **bivalent** nuclear acid ligands binding to; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 79-10-7D, 2-Propenoic acid, polymers 9002-89-5 9004-53-9, Dextrin 12619-70-4, Cyclodextrin 25322-68-3 25322-69-4
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**aptamers** linked by; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 268720-50-9P, RNA (synthetic)
ROLE: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(as ligands to G protein coupled-receptor; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

INDEX TERM: 255916-21-3 255916-22-4
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(neurokinin receptor 1 NK1R epitope; synthesis and identification of **bivalent** binding RNA mols. to G protein-coupled receptors)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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L11 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:5968 CAPLUS
DOCUMENT NUMBER: 130:222045
ENTRY DATE: Entered STN: 06 Jan 1999
TITLE: Anti-L-selectin oligonucleotide ligands recognize CD62L-positive leukocytes: binding affinity and specificity of univalent and **bivalent** ligands

AUTHOR(S): Ringquist, Steven; Parma, David
CORPORATE SOURCE: NeXstar Pharmaceuticals, Inc., Boulder, CO, 80301, USA
SOURCE: Cytometry (1998), 33(4), 394-405
CODEN: CYTODQ; ISSN: 0196-4763
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 15-10 (Immunochemistry)
ABSTRACT:
Oligonucleotide **aptamers** generated against purified LS-Rg, a human L-selectin/IgG fusion protein, bound human CD62L-pos. leukocytes. FACS anal. of lymphocytes or neutrophils stained with fluorescently labeled ***aptamers*** indicated specificity and sensitivity for cellular L-selectin similar to that observed with anti-L-selectin antibody. Univalent ***aptamers*** were compared to **bivalent aptamers** as well as to the anti-adhesion, anti-L-selectin antibody DREG56. Equilibrium and kinetic binding expts. were performed to examine the affinity and kinetic binding parameters of L-selectin **aptamers** to evaluate their binding to CD62L-pos. leukocytes and to test their potential as L-selectin antagonists. Binding expts. indicated that **bivalent aptamers** approached the affinity and the dissociation rate of **bivalent** antibody, and preferentially recognized cellular compared to soluble L-selectin, a potentially useful distinction in vivo. Anti-L-selectin **aptamers** also inhibited L-selectin dependent self-adhesion of neutrophils, suggesting that in vitro univalent and **bivalent aptamers** provided anti-adhesion activity similar to that observed with blocking antibody and indicated a direct blocking mechanism of action during inhibition of L-selectin-dependent trafficking of lymphocytes observed in vivo.

SUPPL. TERM: L selectin oligonucleotide ligand leukocyte
INDEX TERM: Selectins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(L-; anti-L-selectin oligonucleotide ligands recognize CD62L-pos. leukocytes)
INDEX TERM: Leukocyte
(adhesion; anti-L-selectin oligonucleotide ligands recognize CD62L-pos. leukocytes)
INDEX TERM: Leukocyte
Neutrophil
(anti-L-selectin oligonucleotide ligands recognize CD62L-pos. leukocytes)
INDEX TERM: Oligonucleotides
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(anti-L-selectin oligonucleotide ligands recognize CD62L-pos. leukocytes)
INDEX TERM: Cell adhesion
(leukocyte; anti-L-selectin oligonucleotide ligands recognize CD62L-pos. leukocytes)
REFERENCE COUNT: 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD.
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L11 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:650453 CAPLUS
DOCUMENT NUMBER: 127:304108
ENTRY DATE: Entered STN: 13 Oct 1997
TITLE: Antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants
INVENTOR(S): Gabriel, Dean W.
PATENT ASSIGNEE(S): University of Florida, USA
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C12N015-13
SECONDARY: C07K016-12; A01N063-02; A01H005-00
CLASSIFICATION: 3-2 (Biochemical Genetics)
Section cross-reference(s): 5, 10, 11, 15
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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WO 9735980	A1	19971002	WO 1997-US4924	19970325
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9725485	A1	19971017	AU 1997-25485	19970325
EP 889960	A1	19990113	EP 1997-917024	19970325
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9708258	A	19990803	BR 1997-8258	19970325
CN 1232502	A	19991020	CN 1997-194125	19970325
PRIORITY APPLN. INFO.:			US 1996-622538 A	19960325
			WO 1997-US4924 W	19970325

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9735980	ICM	C12N015-13
	ICS	C07K016-12; A01N063-02; A01H005-00
WO 9735980	ECLA	C07K016/12A; C12N015/82C8B6

ABSTRACT:
The subject invention pertains to materials and methods that provide plants with resistance to plant pathogens and pests. Antibodies and **aptamers**

that immunoreact or bind and inhibit the action of protein expression products from avirulence and/or pathogenicity genes, including, but not limited to, the Xanthomonas avr/pth family of such genes, are described. The antibodies of the subject invention function by blocking the action of the primary protein products of avr/pth genes by intercepting and denaturing them prior to their translocation to the plant nucleus. The method of the subject invention concerns transforming a plant with polynucleotide mols. that encode the antibodies. Expression of the antibodies in the plant confers resistance from pathogens and pests. The subject invention also pertains to polynucleotide mols. encoding the subject antibodies, as well as plants and plant tissue transformed with the polynucleotide mols. encoding the subject antibodies.

SUPPL. TERM: avirulence protein antibody plant pathogen resistance; pathogenicity protein antibody plant pathogen resistance; avr gene antibody plant pathogen resistance; pth gene antibody plant pathogen resistance; genetic engineering plant pathogen resistance antibody; Xanthomonas antibody plant pathogen resistance transformation

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(Avr4; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(AvrB101; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(AvrB102; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(AvrB4; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(AvrB6; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study);

PROC (Process); USES (Uses)
(AvrB7; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(AvrBs3; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(AvrXa10; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(AvrXa7; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(PthA; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(PthB; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(PthC; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(PthN; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR

(Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(PthP; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(PthPC; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Disease resistance, plant
Genetic engineering
Plant pathogen
Transformation, genetic
Xanthomonas
(antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Antibodies
Immunoglobulins
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Gene, microbial
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(avr; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Antibodies
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**bivalent**; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(gene avr, avirulence; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(gene pth, pathogenicity; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class

ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(hrpN; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Proteins, specific or class
ROLE: ADV (Adverse effect, including toxicity); AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(hrpZ; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Antibodies
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monovalent; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Antibodies
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nuclear localization signal-comprising; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Denaturation
(protein, by antibody; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Gene, microbial
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(pth; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Plant cell
(transformed; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Dicotyledon (Magnoliopsida)
Monocotyledon (Liliopsida)
Plant (Embryophyta)
Plant tissue
Protoplast and Spheroplast
Seed
Seedling
(transgenic; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Cell nucleus
(translocation of protein to; antibodies against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

INDEX TERM: Recombination, genetic
(translocation, of protein, to nucleus; antibodies

against avirulence/pathogenicity proteins of plant pathogens and use to genetically engineer pathogen resistant plants)

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